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Effects of taurine and/or ginseng and their mixture on lipid profile and some parameters indicative of myocardial status in streptozotocin-diabetic rats

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Abstract This represented study aims to evaluate the protective effects of two natural antioxidants, taurine and/or ginseng and their mixture on lipid profile and some parameters indicative of myocardial status in streptozotocin-diabetic rats.

Adult male albino rats (Sprague Dawley strain) were divided into five groups, a control and four experimental groups; each of them contains five rats. The experimental animals were injected (i.p) with 40 mg/kg body weight of streptozotocin (STZ) daily for 2 successive days to induce diabetes. The first group of diabetic rats was considered as a diabetic group and left without treatment. The second group was injected i.p with 500 mg/kg body weight of taurine daily for one month and served as diabetic plus taurine group. In the third group, ginseng was given orally at a dose of 400 mg/kg body weight daily for the same previous period. The last group received both taurine and ginseng treatments at the aforementioned doses and through the same routes for one month.

The results indicated that the administration of taurine or ginseng showed a remarkable amelioration in glucose, glycosylated hemoglobin (HbA1C), insulin and free T_3 levels. The maximum amelioration in the level of glucose, HbA1C, insulin and free T_3 occurred in diabetic rats that received the mixture of taurine and ginseng. Additionally, treatment of diabetic rats with two antioxidants induced a significant reduction in serum cholesterol, triglycerides and low density lipoprotein levels. The antioxidants also displayed a significant decrease in the activities of cardiac enzymes, aspartate aminotransferase (AST), creatine kinase (CK), lactate dehydrogenase (LDH) and the levels of serum endothelin-1 with a significant elevation in the levels of serum total nitric oxide (TNO) in the diabetic animals group. The results suggest that a combination treatment between taurine and ginseng might represent the treatment of patients with cardiovascular disease (CVD) which is related to diabetic disorder.

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Introduction

Diabetes mellitus is characterized by hyperglycemia and long-term complications affecting the eyes, kidneys, nerves and blood vessels. Several earlier investigations have confirmed the role of oxidative stress in developmental diabetic-mediated

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disorders, possibly *via* the formation of free radicals (Heibashy, 2005; Nogichi, 2007; Manna et al., 2009).

Cardiovascular complications characterized by endothelial dysfunction and accelerated atherosclerosis, are the leading causes of morbidity and mortality associated with diabetes. There is growing evidence that excessive generation of highly reactive free radicals, largely due to hyperglycemia, causes oxidative stress, which further exacerbates the development and progression of diabetes and its complications (Laakso, 1999).

Diabetes mellitus can be chemically induced in animals by the administration of either streptozotocin or alloxan (Like and Rossini, 1976). Streptozotocin, a glucosamine-nitrosourea compound obtained from Streptomyces achromogenes, is used to induce insulin-dependent diabetes mellitus (IDDM) in rodents. Streptozotocin produces cytotoxic effect on β-cells of islets of langerhans of pancreas by interfering with glucose transporter GLUT-2 and causes DNA damage either by alkylation or peroxynitrite formation (Turk et al., 2003). The DNA strands breakage by streptozotocin activates poly (ADP-ribose) polymerase (PARP) and causes ATP depletion, which leads to cell death (Pieper et al., 1999).

Disturbance in lipid metabolism is so prominent that diabetes has been called ''more a disease of lipid than carbohydrate metabolism'' (Rawi et al., 1998). However, the severity of hyperlipidemia associated with diabetes is dependent on the severity of the disturbances in the carbohydrate metabolism and the degree to which the disease is controlled (Betteridge, 1989). Because, glucose cannot be used effectively as a metabolic fuel, the mobilization of energy reserves from fat stores is enhanced, leading to elevated concentration of fatty acids, glycerol and ketones in the blood (Taylor and Aguis, 1988). Over 95% of all lipids transported in the blood are present in lipid-protein or lipoprotein and such types were affected vigorously in diabetes (Osman and Kandil, 1991).

The pathogenesis of diabetes mellitus is managed by oral administration of hypoglycemic drugs. However, these agents have a number of side-effects. Natural antioxidants such as amino acids (taurine) and herbs such as (ginseng) have been used for medicinal purposes for centuries (Olajide et al., 1999).

Taurine is one of the most abundant sulfur containing amino acids. It plays an important role in carbohydrate metabolism, the hypoglycemic properties of taurine were first observed by Ackerman and Heinsen (1935). In addition, taurine was shown by Kulakowski and Maturo (1984) to increase glucose utilization in rats. These results suggested that the hypoglycemia action of taurine on blood glucose level is due to increased glucose uptake followed by increased glycogen accumulation in liver and skeletal muscles. Several authors reported that taurine has the ability to increase insulin stimulated protein synthesis without altering the insulin binding of cells (Heibashy, 2005; El-Nahrawy and Heibashy, 2011).

Moreover, taurine has been shown to influence serum lipid levels by changing lipid metabolism in the liver. Taurine caused a significant hypocholesterolmic effect on rats, probably by enhancing the catabolism of cholesterol and reducing the absorption of dietary cholesterol. Also, the addition of taurine to high cholesterol diet produced a significant reduction, not only in serum total cholesterol and triglyceride levels, but also in total liver cholesterol, lipid and triglyceride contents (Heibashy, 2000, 2005).

Many studies reported that in ischemic heart disease failure, taurine levels in the cytosol were reduced and the external taurine might play an important role as a regulator of cardiac function (Heibashy, 2005; Heibashy and Abdel-Moniem, 2005). Ginseng (*Panax. sp.*) is valuable in Chinese medicine and plays an important role in folk medicine in East Asia. Ginseng glycopeptides have pharmacological effects, e.g., immunomodulatory, anti-tumor, anti-ulcer and hypoglycemic activities. A previous study reported that ginseng contains about 20 ginseng polysaccharides, all of which have anti-hyperglycemic effects (Miyazaki, 1989).

Studies have also shown that ginseng can improve the immune response in diabetic patients (Kiefer and Pantuso, 2003; Cho et al., 2006). Ginseng has been used to treat a wide variety of diseases including anemia, insomnia with neurasthenia, gastritis, blood pressure abnormalities, dyspepsia, overstrain and fatigue due to decrease in blood coagulation and cholesterol and sugar levels (Wesnes et al., 2000; Cho et al., 2006).

Thus, the present study was carried out to investigate the changes in carbohydrate and lipid metabolism associated with disturbances in myocardia as a result of experimentally-induced diabetes. Moreover, the current investigation explored the possible role of taurine or/and ginseng as therapeutic agents to encounter the complications of diabetes.

Material and methods

The experiments were carried out with male albino rats (*Sprague Dawley strain*) weighing 200 ± 5 g. The animals were obtained from Helwan, Cairo, Egypt. The animals were acclimatized for two weeks prior the experiments. They were fed to appetite on standard laboratory animal rodent feed according to NRC (1977) and water was available for animals *ad libitum*. They were housed in a well ventilated animal house kept under standard managerial and environmental conditions (12 h light/dark cycles at 25 ± 2 °C).

Animals were divided into five groups, a control and four experimental groups; each of them contained five rats. The experimental animals were injected (i.p) with 40 mg streptozotocin (STZ) (Sigma Chem. Co., St. Louis, MO, USA)/kg body weight dissolved in citrate buffer (0.1 M, pH 4.5) freshly prepared and injected within five minutes of preparation daily for 2 successive days to induce diabetes. This particular dose of STZ is known to develop metabolic disorders similar to those caused by diabetes mellitus. Blood samples were drawn with a syringe from the tail vein after 24 h of the last injection of STZ for glucose estimation and the animals having a blood glucose level of more than 200 and less than 300 mg/dL were selected for the study (Anjaneyulu and Ramarao, 2002) to achieve resolving the complications accompanied with diabetes.

The first group of diabetic rats was considered as a diabetic group and left without treatment. Each rat of the second group was injected i.p with 500 mg taurine (Sigma Chem. Co., St Louis, MO, USA)/kg body weight for one month and served as diabetic plus taurine group as described by Nanami et al. (1996). The third group, received ginseng (MEPACO, Inshas, Egypt) suspended in tap water orally at a dose of 400 mg/kg-body weight daily for the same previous period. The last group received both taurine and ginseng at the aforementioned doses and through the same routes for one month. At the end of the experimental period, rats were dissected under slight anesthesia, blood samples were collected by heart puncture, centrifuged and the sera were separated and stored at −20 °C.

Estimation of carbohydrate related parameters

Serum glucose concentration was estimated by the enzymatic method of Trinder (1969). Blood glycosylated hemoglobin (HbA1C) was determined by the enzymatic method according to Trivelli's method (Trivelli et al., 1971). Estimation of serum rat insulin levels were assayed according to the methods of Marschner et al. (1974) using ELISA (Sandwich Immunoassay Technique). The commercial kits were purchased from ALPCO (USA).

Estimation of serum hormonal profile

Serum free triiodothyronine (FT_3) and free thyroxin (FT_4) levels were estimated by a radioimmunoassay method kit using solid phase component system according to Ekins (1978) and Siegel et al. (1978). The kits were purchased from Phoenix Co., USA.

Estimation of serum lipid profile

Serum total cholesterol (Watson, 1960), triglycerides (Fossati et al., 1982) and HDL–cholesterol (Freidewald et al., 1972) were estimated enzymatically using commercial kits from Randox, Ltd., Co. (UK). LDL–cholesterol was calculated as per *Freidewald's* equation:

$$\text{LDL–Chol.} = \text{Total Chol.} - [\text{TG}/5 - \text{HDL–Chol.}].$$

Determination of serum cardiac status

Serum activities of lactate dehydrogenase (LDH), creatine kinase (CK) and aspartate aminotransferase (AST) were measured kinetically according to the method of Reitman and Frankel (1957), Szasz et al. (1977) and Weisshaar et al. (1975), respectively. The kinetical commercial kits were purchased from Sclavo Bio-diagnostic Co. (Italy).

Moreover, the concentrations of serum endothelin-1 (Wakisaka et al., 1996) and total nitric oxide (Green et al., 1982) were assayed by ELISA (Sandwich Immunoassay Technique) using commercial kits (IBL-Hamburg, Co., Germany).

Statistic analysis

The comparison between the effects of different antioxidant nutrients on biochemical parameters recorded herein were statistically analyzed using analysis of variance (ANOVA) followed by Duncan's multiple range tests as described by Snedecor and Cochran (1982).

Results and discussion

In the current work, the rat was used as a model for the induction of non-insulin dependent diabetes mellitus (NIDDM) by the injection of the diabetogenic drug streptozotocin (STZ) at a dose level of 40 mg/kg body weight/day for 2 successive days (Nanami et al., 1996). In early studies, several authors reported that administration of STZ to rats induced hyperglycemia and hypoinsulinemia in rats through an accelerated rate of gluconeogenesis (elevated level of hepatic phosphoprotein tyrosine phosphate carboxykinase, pyruvate, carboxylase fructose 1,6 diphosphatase and glucose-6-phosphatase) and depressed rates of glycolysis and pentose shunt (reduced quantity of glucokinase, pyruvate kinase and 6-phosphogluconate dehydrogenase) (Pieper et al., 1999; Turk et al., 2003).

Moreover, the hyperglycemia in STZ-treated rats leads to the formation of hydrogen peroxide, which subsequently generates free radicals such as O^{2-} and OH^{-}. These reactive compounds can cause peroxidation of lipids, resulting in the formation of hydroperoxy fatty acids and endoperoxides (Pushparaj et al., 2000). Also, Coskun et al. (2005) and Cemek et al. (2008) reported that a considerable necrotic degeneration was observed in the peripheral part of the islets of Langerhans in diabetic rats, Okatomoto (1985) discussed the mechanism of action of STZ by acting as alkylating agent to damage the DNA of the pancreatic beta cell. The author also reported that STZ decomposes to form carbonium ions that alkylate DNA and decrease cellular nicotinamide adenine dinucleotide (NAD) level which may adversely affect the beta cell by interrupting respiratory enzyme activity leading to irreversible cellular necrosis.

In agreement with these previously reported results, the current study showed a significant ($p < 0.05$) elevation in glucose, glycosylated hemoglobin (HbA1C) levels and a significant ($p < 0.05$) decrease in the concentration of insulin in serum (Table 1). These results are attributed to the destructive effect of STZ on the beta cells of pancreatic islets which led to inhibition of insulin synthesis and increased blood glucose level due to reduced entry of glucose into peripheral tissues, muscles and adipose tissue (Masashi and Olefsky, 1979), increased glycogen breakdown (Gold, 1970) and increased hepatic glucose output either by enhanced glycogenolysis and/or gluconeogenesis (Rawi et al., 1996).

Furthermore, glycosylated hemoglobin (HbA1C) is normally high in diabetic patients and can reflect their metabolic control and is considered a useful method in this regard. HbA_{1C} is produced by non-enzymatic condensation of glucose molecules with free amino acids on the globin component of hemoglobin (Beissuenger et al., 1993). The high level of glucose led to an elevation in HbA1C (Nathan, 1990). HbA1C is useful in the demonstration of glycemic control over a period of 8–12 weeks, which is the life span of RBC_S (Heibashy, 2005). Its main disadvantage is that it is not known until now whether stable HbA1C can undergo rapid changes induced by short time variation in glucose concentration (Delnero et al., 1990). Also, false higher results may be obtained from uremia or acylated hemoglobin resulting from high aspirin doses, also low results are obtained with short life span of RBC_S as with hemolytic anemia (Boucher et al., 1983).

Taurine is a considerably potent hypoglycemic agent. Regarding its hypoglycemic effect, it was suggested that an insulin receptor is the postulated site of action of taurine (Kulakowski and Maturo, 1990), taurine enhances glycogenesis, glycolysis and glucose oxidation (Mozaffari et al., 1986), ameliorates the hyperglycemia induced by STZ (El-Agousa et al., 2000) and lastly it was also used as adjuvant therapy in patients with IDDM (Elizarova and Nedosugova, 1996). These results are in agreement with the present finding reflected by reducing levels of glucose and HbA1C and the elevation of insulin concentration in rats treated with taurine for one month (Table 1).

Ginseng has been shown to inhibit gastric secretion in rats and to decrease glucose and maltose absorption in rats and humans. Also, ginseng was reported to slow digestion, so low lev-

Table 1 Effects of taurine or/and ginseng on serum glucose, insulin, FT_3 and FT_4 levels and HbA_{1C} concentration in streptozotocin-diabetic rats.

Treatment Groups	Glucose (mg/dL)	HbA_{1C} (%)	Insulin (ng/ml)	FT_3 (pg/ml)	FT_4 (ng/dL)
Control	112.63 ± 3.59^{A}	4.88 ± 0.45^{A}	1.66 ± 0.019^{A}	0.82 ± 0.016^{A}	0.43 ± 0.009
Diabetic	269.55 ± 6.41^{B}	8.54 ± 0.79^{B}	0.34 ± 0.007^{B}	0.49 ± 0.009^{B}	0.42 ± 0.008
Diabetic + T	196.23 ± 4.72^{C}	6.61 ± 0.63^{C}	0.62 ± 0.011^{C}	0.64 ± 0.011^{C}	0.43 ± 0.009
Diabetic + G	217.27 ± 5.16^{D}	7.02 ± 0.70^{D}	0.44 ± 0.009^{D}	0.52 ± 0.011^{C}	0.43 ± 0.009
Diabetic + T + G	168.91 ± 4.39^{E}	5.23 ± 0.52^{E}	0.98 ± 0.014^{E}	0.71 ± 0.013^{D}	0.43 ± 0.009

Values are expressed as means ± S.E.
A, B, C, D, E = means bearing different superscripts within the same row that differ significantly ($P < 0.05$).

els of blood glucose were recorded. Furthermore, both of which operate through delaying or inhibiting the absorption of carbohydrates in the gut. The effect of ginseng in lowering blood glucose level in STZ-diabetic rats is probably attributed to the insulin like components present in this plant (Vuksan et al., 2001).

Active components of ginseng that may have an important mediating role in the hypoglycemic processes include its polysaccharide (ginsenans), peptidoglycan (panaxans), and ginsenoside profiles. Most pharmacological actions of ginseng, however, are attributed to the involvement of ginsenosides (Kim et al., 2002). Moram (2001) stated that ginseng fractions isolated from ginseng roots such as ginseng polysaccharides or polypeptides reduced blood glucose level and stimulated the release of insulin. They suggested that ginseng increases carbohydrate utilization and promotes the aerobic oxidation course.

Moreover, Attele et al. (2002) suggested that the antidiabetic action of ginseng fraction may be partially mediated through a decrease in hepatic gluconeogenesis by suppressing the activity of key glucogenic enzymes. Also, ginseng has been shown to increase glucose-transporter-2 in the livers of normal and hyperglycemic mice.

In agreement with these previously reported results, the current study showed a remarkable amelioration in glucose, glycosylated hemoglobin (HbA1C) and insulin levels (Table 1). However, the maximum amelioration in the levels of glucose, HbA1C and insulin occurred in diabetic rats which received the mixture of taurine and ginseng. These results may be attributed to the additive or complementary effects of the hypoglycemic agents for taurine and ginseng.

In the current work, the reciprocal relationship between the concentrations of thyroid hormones (FT_3 and FT_4) in serum and hyperlipidemia is described. These results seemed to be in complete accordance with earlier studies made by Long et al. (1953) they observed that thyroid activity has an adverse effect on all plasma lipids.

The choice of serum free T_3 and free T_4 as the best *in vitro* tests of thyroid function was based on the following fact: serum free T_3 and free T_4 concentrations may be expected to reflect the actual thyroid status more than the total T_3 (TT_3) and total T_4 (TT_4) concentrations because of the dependence of TT_3 and TT_4 values on plasma protein binding which almost binds all thyroid hormones liberated from the thyroid gland leaving free T_3 and free T_4 relatively unchanged in healthy subjects.

From Table 1, a significant ($p < 0.05$) decrease in the level of free T_3 was evoked in the diabetic group while, a numerical change occurred in the level of free T_4. These results may be due to the conversion of T_3 to T_4 or/and conversion of reverse T_3 (rT_3) to T_4. The Free T_3 is considered to be the major biologic mediator of the thyroid function test. The obtained data in the current investigation were confirmed by several recent researches (Heibashy et al., 2009)

By reviewing the data in Table 2, the data revealed a proportional relationship between the severity of hyperlipidemic effect of STZ and the hypoglycemic status of the experimental animals. A mountain of research was done and all of them pointed to marked elevation in all lipid fractions except HDL–cholesterol which showed negative correlation with the severity of diabetes (Nanami et al., 1996; You and Chang, 1998). The diabetic hyperlipidemia is attributed to the disturbance of hormonal regulation of glucose metabolism and leptin level. The elevated level of serum triglycerides in diabetic animals may be attributed to a decrease in the clearance and production of the major transporters of endogenously synthesized triglycerides (Abdel-Moneim, 1998). This decrease of clearance was found to be due to the decrease in adipose tissue lipoprotein lipase as demonstrated in human diabetics (Nikkila et al., 1977) and a decrease in hepatic triglycerides lipase as indicated in STZ-diabetic rats (Nakai et al., 1979). Also, the expansion of cholesterol pool in diabetes was explained by O'Meara et al. (1990) through the increased intestinal cholesterol synthesis, and the diminished synthesis of bile salts due

Table 2 Effects of taurine or/ and ginseng on serum lipid profile in streptozotocin-diabetic rats.

Treatment groups	Triglyceride (mg/dL)	Cholesterol (mg/dL)	HDL–cholesterol (mg/dL)	LDL–cholesterol (mg/dL)
Control	61.14 ± 2.39^{A}	54.33 ± 2.07^{A}	15.29 ± 0.86^{A}	26.81 ± 1.29^{A}
Diabetic	129.77 ± 3.97^{B}	97.58 ± 4.62^{B}	11.54 ± 0.59^{B}	60.09 ± 2.11^{B}
Diabetic + T	83.57 ± 3.52^{C}	76.91 ± 3.74^{C}	13.68 ± 0.68^{C}	46.52 ± 1.68^{C}
Diabetic + G	102.63 ± 3.77^{D}	80.87 ± 4.16^{D}	13.44 ± 0.67^{C}	46.90 ± 1.69^{C}
Diabetic + T + G	72.18 ± 2.61^{E}	65.26 ± 2.85^{E}	15.23 ± 0.83^{D}	35.59 ± 1.42^{D}

Values are expressed as means ± S.E.
A, B, C, D, E = means bearing different superscripts within the same row that differ significantly ($P < 0.05$).

Table 3 Effects of taurine or/and ginseng on serum cardiac enzyme activities and the levels of endothelin-1 and TNO in streptozotocin-diabetic rats.

Treatment groups	LDH (U/L)	CK (U/L)	AST (U/L)	Endothelin-1 (pg/ml)	TNO (μmol/L)
Control	235.11 ± 7.12^{A}	92.56 ± 2.81^{A}	121.54 ± 4.59^{A}	0.38 ± 0.007^{A}	54.27 ± 2.17^{A}
Diabetic	387.42 ± 11.26^{B}	174.03 ± 4.32^{B}	197.66 ± 7.11^{B}	0.81 ± 0.016^{B}	28.39 ± 1.26^{B}
Diabetic + T	303.55 ± 10.27^{C}	112.67 ± 3.74^{C}	158.83 ± 6.23^{C}	0.61 ± 0.013^{C}	38.61 ± 1.68^{C}
Diabetic + G	305.61 ± 11.94^{C}	110.94 ± 3.82^{C}	171.04 ± 6.84^{D}	0.69 ± 0.014^{D}	35.59 ± 1.53^{D}
Diabetic + T + G	271.06 ± 8.87^{D}	98.51 ± 3.56^{D}	140.23 ± 5.02^{E}	0.55 ± 0.010^{E}	45.48 ± 1.94^{E}

Values are expressed as means ± S.E.
A, B, C, D, E = means bearing different superscripts within the same row that differ significantly ($P < 0.05$).

to decreased hepatic phenol-2-monooxygenase activity, the key enzyme responsible for the catabolism of cholesterol to bile acids. LDL–cholesterol elevation in the serum of diabetic rats could be attributed to a diminished number of peripheral LDL receptors or reduced LDL binding to its receptors (Betteridge, 1989; Osman and Kandil, 1991). So, the hyperlipidemic pattern observed in this study after the induction of diabetes by STZ was in accordance with the previously published literature. This pattern is called atherogenic pattern of hyperlipidemia due to its perception of arteriosclerosis (Davidson, 1998).

The treatment of diabetic rats with taurine induced a marked decrease in lipid profile except HDL–cholesterol which exhibited a value higher than that recorded in STZ diabetic animals (Table 2). A similar study found that oral taurine administration lowered the serum cholesterol, triglyceride and total lipid levels as well as liver phospholipid and lipid contents in rats (Mochizuki et al., 1998). The authors attributed the reduction in liver triglyceride content to the inhibition of diacylglycerol, acyl-CoA synthetase and diacylglycerol acyltransferase by taurine treatment. These results are in agreement with those obtained by Heibashy (2000) and Heibashy et al. (2009).

Taurine suppressed the increase in the concentration of serum total cholesterol and triglycerides in hypercholesterolemic stork-prone spontaneously hypertensive rats (Ogawa, 1996). The authors suggested that the hypolipidemic effect of taurine was partly due to the inhibition of cholesterol absorption in the intestine. Besides this action, cholesterol elimination from the body was also postulated as an important factor by which taurine reduces tissues and serum cholesterol levels through increasing the conversion of cholesterol to bile acid as a result of enhancement of 7-α hydroxylase, the rate limiting enzyme of hepatic cholesterol catabolism and its conjugation to bile acids lately. Furthermore, it has been suggested that taurine may be responsible for the increase of HDL, modification cholesterol synthesis in the liver or/and balance of each of the serum lipoprotein fractions containing cholesterol (Heibashy, 2000). Moreover, it is likely possible that chronic administration of taurine may be responsible also for hypocholesterolemia by the enhancement of LDL receptor binding in the liver (Kamata et al., 1996).

Maximum amelioration occurred in the total cholesterol, HDL, LDL and triglycerides of diabetic rats treated with the mixture of taurine and ginseng. These results may be attributed to the powerful joint effects of both antioxidants which also act as hypolipidemic agents.

It is a well-established fact that diabetes is a risk factor for cardiovascular disease. While, microvascular complications of diabetes include nephropathy and retinopathy, macrovascular complications resulting in atherosclerotic cardiovascular diseases such as coronary artery disease, cerebrovascular disease and peripheral vascular disease are the leading causes of death in the diabetic population (Laakso, 1999). The Diabetes Control and Complications trial (1993) demonstrated that tight control of blood glucose is effective in reducing clinical complications significantly, but even optimal control of blood glucose could not prevent complications suggesting that alternative treatment strategies are needed. Since, numerous studies demonstrated that oxidative stress, mediated mainly by hyperglycemia-induced generation of free radicals contributes to the development and progression of diabetes and related contributions, it became clear that ameliorating oxidative stress through treatment with antioxidants might be an effective strategy for reducing diabetic complications (Heibashy, 2005).

There was a significant ($p < 0.05$) elevation in the activities of cardiac enzymes (AST, CK and LDH) in diabetic rats group (Table 3). These results may be due to the excessive myocardial infraction as a result of free radical production, epigenetic gene alteration and inhibition in the activity of total nitric synthase (NOs) enzyme which led to a remarkable depletion in the concentration of total nitric oxide in the blood. Also, these changes may be due to the increase in the level of serum endothelin-1 accompanied with elevation in serum ADMA level and appearance of hypertension and metabolic syndrome. These results are in parallel with those obtained by Heibashy (2005) and Karaca et al. (2010).

In the current work, the maximum improvement occurred in cardiac status parameters, (AST), (CK) and (LDH) activities and the levels of serum endothelin-1 and TNO in the diabetic animals group which was treated with both taurine and ginseng. These data may be due to the synergistic effects of both antioxidants by improving their pharmadynamic and pharmakinetic properties, so they are considered bio-tonic agents. So, a combination of taurine and ginseng might represent the treatment of patients with cardiovascular diseases (CVD) which is related to diabetic disorders.

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